REMARKS

Applicant respectfully requests reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow.

I. Disposition of Claims

Claims 1-19 and 22-47 are pending, with claims 1-19 and 22-42 withdrawn. Claims 20-21 are canceled. Claim 43 is amended. No new matter has been added as the result of the amendment. Support for amended claim 43 can be found in the claim as originally filed. Upon entry of the amendment, claims 43-47 will be pending for examination on the merits.

II. Claim Rejection – Enablement

Claims 43-47 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly not complying with the enablement requirement. Office Action, pp. 2-9. Specifically, the Office Action states that the instant claims, while enabled for PM-1 and MR16-1 antibodies for treating inflammatory bowel disease, are not enabled for all antibodies to treat the same. To support this ground of rejection, the Office Action states that the specification does not provide examples outside of PM-1 and MR16-1 antibodies. *Id.* Additionally, the Office Action cites to Chuntharapai *et al.*, *Methods in Enzymology*, 288: 15-27 ("Chuntharapai"), which allegedly describes the state of the art with respect to antibodies. *Id.* at pg. 9. Applicants respectfully traverse this ground of rejection.

The specification fully enables the invention for using more than just the PM-1 and MR16-1 antibodies. Applicants respectfully direct the Examiner's attention to the specification on page 37, lines 15-31, stating, "[t]he activity of the IL-6 antagonist for use in the present invention can be evaluated using a ***conventionally known method***...[i]n the above assay system, a negative control group containing no IL-6 antagonists, in addition to the group in which an IL-6 receptor antagonist is present, is set up, and the results obtained for them are compared to evaluate the IL-6 inhibiting activity of the IL-6 receptor antagonist" [emphasis added]. The specification acknowledges, therefore, that the skilled artisan would have only needed to apply routine, commonly known methods to determine applicable IL-6 antagonists. Although this process may constitute experimentation, it hardly rises to the level

of "undue experimentation" under the enablement requirement. Consequently, because one skilled in the art would have to perform "undue experimentation" to determine appropriate antibodies in addition to PM-1 and MR16-1, the claims do not lack enablement for all *anti-interleukin-6 receptor antibodies which bind to interleukin-6 receptor, block signal transduction by IL-6 and inhibit the biological activity of IL-6*, as claimed.

Moreover, the Office Action's reliance on Chuntharapai is improper, given all that Chuntharapai teaches. On page 22 of Chuntharapai, the reference teaches that "[o]ne can select antagonistic MAbs to a particular receptor by determining their abilities to inhibit bioactivities of the relevant ligand." This description points to the fact that one skilled in the art would appreciate how to identify appropriate MAbs, based on their bioactivity. Accordingly, this statement supports the specification's statement, described *supra*, that one skilled in the art would be capable of determining appropriate *anti-interleukin-6 receptor antibody*, as claimed. Indeed, the claims are directed to such an antibody with the following properties recited therein: *binds to interleukin-6 receptor, blocks signal transduction by IL-6 and inhibits the biological activity of IL-6.* Based on an understanding of Chuntharapai, and supported by the present specification, one skilled in the art would not need to perform "undue experimentation" in identifying the appropriate anti-interleukin-6 receptors for treating inflammatory bowel disease.

Applicants, therefore, respectfully request that the enablement rejection of claims 43-47 be withdrawn.

III. Claim Rejection – Indefiniteness

Claims 43-47 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly vague and indefinite. Office Action, pp. 9-10. Applicants respectfully submit that, considering the claim amendments, claims 43-47 are not indefinite. Applicants, therefore, respectfully request that the rejection of claims 43-47 be withdrawn.

IV. Claim Rejection – Prior Art Anticipation

a. The Burstein reference

Claims 43-44 and 47 are rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Burstein (WO 96/38481) ("Burstein"). Office Action, pg. 11. Applicants respectfully traverse this ground of rejection.

To anticipate a claim, a single prior art reference must expressly or inherently teach every element of the claim. *See* MPEP 2131. Here, Burstein fails to teach each and every element of the claimed invention.

Claim 43 is directed to a method of treating inflammatory bowel disease and recites *administering an **anti-interleukin-6 receptor antibody** which **binds to interleukin-6 receptor**, blocks signal transduction by IL-6 and inhibits the biological activity of IL-6.* As described in the specification, interleukin-6 transmits its biological signal through two proteins on a cell, IL-6 receptor and gp130. *See* Specification, pp. 1-2. In operation, IL-6 binds to an IL-6 receptor to form an IL-6/IL-6 receptor complex, and the complex then binds to gp130. *Id.* Both IL-6 receptor and gp130 have specific antibodies. *Id.* at pg. 2. While these antibodies are both considered IL-6 antagonists, they are distinct to their specific receptors, i.e., either IL-6 or gp130. *Id.* Correspondingly, since claim 43 is directed specifically to an anti-interleukin-6 receptor antibody that binds to an interleukin-6 receptor, a reference that fails to teach this process is not anticipatory.

Burstein does not describe the step of binding an anti-IL-6 receptor antibody to an IL-6 receptor. Indeed, Burstein focuses on antibodies to gp130. *See* Burstein, abstract and pg. 4, ll. 23-30. The Office Action, while recognizing Burstein's omission, opines that since the claim recites "comprising" language, the scope of the claim encompasses blocking signal through receptors other than an IL-6 receptor. Office Action, pg. 11. This rationale, however, fails to satisfy the requirement that an anticipatory reference must teach each and every element of the claim set forth by MPEP 2131, as described *supra*. Here, the claim specifically recites that an anti-interleukin-6 receptor antibody binds to ***interleukin-6 receptor***. The claimed antibody is, therefore, specific for IL-6 receptor and binds to IL-6 receptor. Since Burstein describes only antibodies to gp130, the reference does not teach the claimed step of binding to an IL-6 receptor. Regardless of the notion that other mechanisms may hinder IL-6 signal transmission, since Burstein does not teach the claimed element of

binding an IL-6 receptor antibody to an IL-6 receptor, claim 43, and its dependents, are not anticipated.

Applicants, therefore, respectfully request that the rejection of claims 43-44 and 47 be withdrawn.

b. The Kishimoto reference

Claims 43-44 are rejected under 35 U.S.C. § 102(e) as allegedly anticipated by Kishimoto *et al.* (US 5,888,510) ("Kishimoto"). Office Action pp. 11-12. Applicants respectfully traverse this ground of rejection.

As describe *supra*, a reference is an anticipatory reference against a claim only if the reference teaches each and every element of the claim. *See* MPEP 2131. Applicants respectfully submit that Kishimoto does not teach all elements of the instant claims. In particular, Kishimoto does not teach a method for treating ***inflammatory bowel disease***, as claimed, or the step of administering to a subject in need of such treatment.

Kishimoto is directed to a method for treating chronic rheumatoid arthritis by administering an IL-6 antagonist. *See* Kishimoto, col. 13-14. While rheumatoid arthritis may include a inflammation in joints, Kishimoto does not describe methods of treating other types of inflammation that are distinct from rheumatoid arthritis. Indeed, Kishimoto does not even mention inflammatory bowel disease. The rejection does not suggest any links between these diseases.

Accordingly, since Kishimoto does not teach each and every element of the claim, Kishimoto is not an anticipatory reference. Applicants, therefore, respectfully request that the rejection of claims 43-44 be withdrawn.

IV. Claim Rejection – Prior Art Obviousness

a. Burstein in view of Queen

Claims 43-47 are rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Burstein in view of Queen *et al.* (US 5,530,101) ("Queen"). Office Action, pg. 13. Applicants respectfully traverse this ground of rejection.

Burstein has been described *supra*, along with reasons why Burstein is not an anticipatory reference. Queen does not remedy the deficiencies of Burstein.

Queen is directed to chimeric and humanized antibodies. *See* Queen, abstract and reference as a whole. Queen, however, does not describe treating inflammatory bowel disease by *administering an anti-interleukin-6 receptor antibody which binds to interleukin-6 receptor, blocks signal transduction by IL-6 and inhibits the biological activity of IL-6*, as claimed. Indeed, Queen does not even mention an IL-6 receptor, much less treating inflammatory bowel disease by administering an antibody to an IL-6 receptor. Both Burstein and Queen, therefore, fail to teach that an antibody binding to an IL-6 receptor, as administered to a patient, would treat inflammatory bowel disease. Moreover, neither reference fairly suggests that the teachings of either reference can be extended to encompass the claimed antibody binding to an IL-6 receptor. Hence, one skilled in the art reading Queen and Burstein, either singly or in combination, would not find the claimed method obvious.

Applicants, therefore, respectfully request that the rejection of claims 43-47 over Burstein in view of Queen be withdrawn.

b. Kishimoto in view of Queen

Claims 43-47 are rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Kishimoto in view of Queen. Office Action, pp. 13-14. Applicants respectfully traverse this ground of rejection.

Kishimoto has been described *supra*, along with reasons why Kishimoto is not an anticipatory reference. Queen does not remedy the deficiencies of Kishimoto.

Queen has been described *supra*. In addition, Queen does not describe a method of treating *inflammatory bowel disease*, as claimed. Moreover, a fair reading of Queen would not lead one skilled in the art to find it obvious to administer an antibody to an IL-6 receptor

for treating inflammatory bowel disease, as claimed. Since neither Kishimoto nor Queen fairly suggest this method, the combination of the two references, therefore, also fail to suggest treating inflammatory bowel disease by administering an antibody to an IL-6 receptor, as claimed.

Applicants, hence, respectfully request that the rejection of claims 43-47 over Kishimoto in view of Queen be withdrawn.

V. Conclusion

Applicant believes that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing or a credit card payment form being unsigned, providing incorrect information resulting in a rejected credit card transaction, or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

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FOLEY & LARDNER LLP
Customer Number: 22428
Telephone: (202) 672-5569
Facsimile: (202) 672-5399

Stephen B. Maebius
Attorney for Applicant
Registration No. 35,264